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Percutaneous Revascularization for Stable Coronary Artery Disease

Temporal Trends and Impact of Drug-Eluting Stents

We read with great interest the paper by Hilliard et al. (1) in *JACC: Cardiovascular Interventions* and congratulate the investigators on a very well-done and important analysis. Many of those who have criticized the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) study as not being "generalizable" to contemporary clinical practice (e.g., only 6% of screened patients were randomized, percutaneous coronary intervention [PCI] was substandard, too many patients enrolled from Veterans Affairs and Canada, very low rate of drug-eluting stent usage, adherence to optimal medical therapy was not achievable in the real world) should be reassured by the Mayo Clinic data. The Mayo data indicate that procedural success and technical proficiency continue to evolve and improve, in-hospital mortality and target vessel revascularization continue to decline, and results achievable in the real world might even be better if more robust optimal medical therapy were more widely embraced and used.

The fact that the rates of death, death/myocardial infarction (MI), and revascularization in COURAGE at 4.6 years are virtually identical to the rates reported from Mayo at 4 years supports the concept suggested by the results of COURAGE that these late events (and need for subsequent revascularization) are not being driven by the stenoses that are initially "being fixed," but rather by new plaque ruptures in non-flow-limiting vessels. Moreover, we note that the patient population undergoing PCI at Mayo between 1997 and 2003 was remarkably similar to patients enrolled in COURAGE during the same time period. Table 4 of Hilliard et al. (1) cites certain baseline characteristics of the Mayo population that were higher risk than those of the COURAGE population, but the investigators do not comment on the higher rates of diabetes (32% vs. 24%), multivessel coronary artery disease (69% vs. 51%), and left anterior descending coronary artery disease (68% vs. 47%) in the COURAGE PCI cohort as compared with the Mayo patients (2,3). Additionally, in their Table 1 (1), only 13% of patients in the Mayo Clinic cohort had a positive stress test as the predominant indication for PCI, whereas in COURAGE, all patients had objective evidence of myocardial ischemia (2,3). Thus, when a more comprehensive list of characteristics is analyzed it appears the Mayo and COURAGE PCI cohorts were indeed very comparable populations of North American stable angina patients. This is underscored further by the performance and outcomes of the PCI procedures that were very comparable in both studies and similar to contemporary practice in the National Cardiovascular Data Registry (4). The difference in procedural success noted in Table 4 (89% vs. 94%) of Hilliard et al. (1) is likely due to differing definitions (COURAGE excluded all periprocedural MIs whereas Mayo only excluded Q-wave MIs).

Based on these important observational data from a center widely acknowledged for excellence in PCI and which serves to validate the quality of PCI in COURAGE, there can no longer be any debate that optimal medical therapy is the cornerstone of management for all patients with stable coronary artery disease and should be the initial management strategy as concluded by the COURAGE study. We also enthusiastically concur with Hilliard et al. (1) that contemporary PCI is even safer and more efficacious than in the bare-metal stent era and is an important complement to optimal medical therapy for symptom relief in patients with angina that cannot be controlled by medications. Despite these advances, it is also noteworthy to emphasize that there has been no change in the unadjusted rates of mortality or the combined end point of death or MI in the drug-eluting stent era (2003 to 2006) as compared with the bare-metal stent era (1997 to 2003) in the Mayo observational experience. Lastly, the hypothesis that coronary revascularization improves prognosis in patients with severe ischemia is intriguing, but remains unproven, and must be evaluated in a rigorously designed and performed randomized clinical trial.

***Steven P. Sedlis, MD**
William E. Boden, MD

*Veterans Affairs (VA) New York Harbor Health Care System and New York University School of Medicine
423 East 23rd Street
New York, New York 10010
E-mail: Steven.Sedlis@med.va.gov

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Reply

We thank Drs. Sedlis and Boden for their interest in our article in *JACC: Cardiovascular Interventions* (1). Although we agree that our study suggests that "COURAGE-like" results are being achieved in clinical practice, the analysis was not intended to investigate the generalizability of the trial (1,2). It is reasonable to propose that

outcomes would be even better if "optimal medical therapy," as administered in the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) study, was used, though this requires additional resources to establish an intense case management approach.

We thank Drs. Sedlis and Boden for highlighting the fact that there were additional differences between our cohort and that of the trial; however, it is not possible to accurately compare the risk profiles of the 2 groups. That said, the (mean) age, one of the most important determinants of procedural risk and long-term outcomes, was 5 years greater in the Mayo Clinic cohort. Drs. Sedlis and Boden also state that a minority of our cohort had a positive stress test. This is not accurate. Thirteen percent of patients had a positive stress as the predominant indication for percutaneous coronary intervention (PCI), but other patients also had positive stress tests but this was not the primary indication for referral and therefore not included in the variable they quote. Fifty percent of our cohort had Canadian Cardiovascular Society class III/IV angina indicating that these patients had a significant ischemic burden, and thus, we do not concur with the conclusion of Drs. Sedlis and Boden that the Mayo Clinic registry and COURAGE trial cohorts were comparable with respect to their risk profile.

Differences in procedural success may, in part, have been due to the definitions used. Drs. Sedlis and Boden point out that in COURAGE, "all periprocedural MIs" were excluded. However, clinical success (equating to our procedural success) was defined as angiographic success plus the absence of in-hospital myocardial infarction (some likely to be procedural myocardial infarction in an elective PCI population), emergency coronary artery bypass graft, or death in COURAGE.

Stable coronary artery disease represents a wide spectrum of patients with heterogeneous severity of symptoms and risk. Thus, we do not support the recommendation that all patients with stable coronary artery disease should initially be managed with medical therapy (3). This is important because patients in COURAGE were randomized after coronary angiography was performed. High-risk patients, such as those with class IV angina, markedly positive stress test, refractory heart failure, cardiogenic shock, and an ejection fraction of less than 30% were excluded. Therefore, we recommend that the decision regarding medical therapy versus PCI should be based on the severity of symptoms and risk stratification. It is our belief that PCI is very effective in treating angina and improving functional status, and medical therapy is not superior to PCI in the management of stable coronary artery disease (3).

We agree that the use of drug-eluting stents (DES) does not reduce the likelihood of death of myocardial infarction, but DES reduce the need for target lesion revascularization. As such, there is a distinct possibility that symptom control would have been superior in the PCI arm of COURAGE had DES been used. Twenty-one percent of the PCI group required repeat revascularization during follow-up, a rate that would have likely been significantly lower had DES been used. Thus, the superiority of PCI with respect to improved relief in angina in the COURAGE may have been sustained for a longer period with DES use.

***Abhiram Prasad, MD**
Anthony Hilliard, MD

*Cardiac Catheterization Laboratory
Mayo Clinic
200 First Street SW
Rochester, Minnesota 55905
E-mail: prasad.abhiram@mayo.edu

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